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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/731,419	12/09/2003	Bassem A. Bejjani	SH1-001US	3921

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EXAMINER	
THOMAS, DAVID C	

ART UNIT	PAPER NUMBER
1637	

DATE MAILED: 03/21/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/731,419	BEJJANI ET AL.	
	Examiner	Art Unit	
	David C. Thomas	1637	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☐ Responsive to communication(s) filed on *01 March 2006*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1,2,4,5,7-9,11,16,21-23,28,51-53 and 71-74* is/are pending in the application.

4a) Of the above claim(s) *51-53* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1,2,4,5,7-9,11,16,21-23,28 and 71-74* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Election/Restrictions

1. Applicant's election with traverse of Group 1, claims 1, 2, 4, 5, 7-9, 11, 16, 21-23, 28, and 71-74 in the reply filed on March 1, 2006 is acknowledged. Claims 51-53 are withdrawn from further prosecution. The traversal is on the grounds that there is no burden searching both groups. This is not found persuasive for several reasons. First, the separate classification of the two groups is prima facie evidence of burden, which evidence has been rebutted. Second, the search for the product claims (tagged reference genes including a cystic fibrosis transmembrane conductance regulator gene) is an entirely distinct search from the method claims, since the prior art which may be used to reject product claims are often entirely unrelated references which share common products.

The requirement is still deemed proper and is therefore made FINAL.

Claim Rejections - 35 USC § 102

2. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

3. Claims 1, 2, 4, 5, 7-9, 11, 16, 21-23, 28, and 71-74 are rejected under 35 U.S.C. 102(b) as being anticipated by Chenchik et al., (U.S. Patent No. 5,759,822).

Chenchik teaches a method, comprising: synthesizing one or more nucleic acid sequences (by amplification of DNA fractions or by digestion of DNA with restriction

endonucleases, column 11, lines 62-67), each relevant for use as a clinical reference (either normalized cDNA populations, column 13, lines 9-12 or cDNA libraries, column 13, lines 44-48); tagging at least one end of each sequence for amplification by a primer (ligation of adapters, column 13, lines 12-15 and lines 53-56 and Figures 1); and amplifying the one or more nucleic acid sequences using the primer (column 14, lines 5-6).

With regard to claim 2, Chenchik teaches a method, wherein the tagging includes attaching an additional sequence of nucleotides, wherein the additional sequence is complementary or identical to a nucleotide sequence of the primer (column 13, lines 12-15, lines 53-56, column 14, lines 5-6 and Figure 1).

With regard to claim 4, Chenchik teaches a method, wherein the tagging includes attaching a first sequence of nucleotides to a first end of each of the one or more synthesized nucleic acid sequences (Figure 1, top left side), wherein the first sequence is complementary to a nucleotide sequence of a first primer set (column 14, lines 5-6), and the tagging includes attaching a second sequence of nucleotides to a second end of each of the one or more synthesized nucleic acid sequences (Figure 1, top right side), wherein the second sequence is identical to a nucleotide sequence of a second primer of a primer set (column 14, lines 5-6).

With regard to claim 5, Chenchik teaches a method, wherein the synthesizing comprises synthesizing two complementary nucleic acid strands (by amplification using sequence-specific PCR primers, column 11, lines 62-67), wherein: a first strand includes a first nucleic acid sequence relevant for clinical reference and a nucleic acid

tag complementary to a first primer of a primer set (added by ligation, column 13, lines 12-15 and lines 53-56) and a second strand includes a nucleic acid sequence complementary to the first strand and a nucleic acid tag complementary to a second primer of a primer set (added by ligation, column 13, lines 12-15 and lines 53-56).

With regard to claim 7, Chenchik teaches a method, wherein at least one of the one or more synthesized nucleic acid sequences includes at least one mutation of a nucleotide in a normal human nucleic acid (partially homologous sequences, column 12, lines 28-30 or those with mutations, column 12, line 66 to column 13, line 8; see Example 4 for example of human nucleic acid, skeletal muscle, column 24, lines 8-25).

With regard to claim 8, Chenchik teaches a method, further comprising synthesizing multiple mixtures of at least one reference nucleic acid apiece (such as obtained by digestion with a restriction endonuclease, column 11, lines 62-67), wherein: each of the multiple mixtures has an associated primer set (Figure 2, both mixtures use primers a and b), and wherein: each member of one of the multiple mixtures includes a first tag attached to a first end of the member, wherein: the first tag comprises a sequence of nucleotides complementary to a nucleotide sequence of a first primer of the associated primer set (Figure 2, second section and column 13, lines 12-15 and lines 53-56), and each member includes a second tag attached to a second end of the member, wherein: the second tag comprises a sequence of nucleotides identical to a nucleotide sequence of a second primer of the associated primer set (Figure 2, second section and column 13, lines 12-15 and lines 53-56).

With regard to claim 9, Chenchik teaches a method, further comprising combining each of the multiple mixtures with each other and separately controlling each of the multiple mixtures to achieve separate amounts of amplification for each of the multiple mixtures of components (Figure 2, third section, combining of mixtures and controlling amplification depending on formation of pan structures, bottom and column 13, line 67 to column 14, line 9).

With regard to claim 11, Chenchik teaches a method, wherein separately controlling each of the multiple mixtures includes controlling a physical characteristic of a combined mixture of the multiple mixtures to favor an amplification capability of one primer set over an amplification capability of another primer set (primer set is prevented from binding to one mixture which forms pan structure, but effectively binds to other mixture, column 14, lines 7-9, and Figure 2, bottom).

With regard to claim 16, Chenchik teaches a method, further comprising adding normal human nucleic acid to the one or more synthesized nucleic sequences relevant for clinical reference in order to achieve a mixture of the nucleic acids representing at least a segment of homologous heterozygous alleles (use of human skeletal muscle cDNA will include normal DNA, which is then used for library construction by adapter ligation and PCR, Example 4, lines 5-25).

With regard to claim 21, Chenchik teaches a method, further comprising joining multiple nucleic acid segments using a ligation extension to perform the synthesizing of one or more reference nucleic acid sequences (ligation of adapters, column 13, lines 12-15 and lines 53-56).

With regard to claim 22, Chenchik teaches a method, wherein for at least one of the reference nucleic acids, the synthesizing includes: synthesizing a first nucleic acid that includes a first end comprising a base sequence complementary to the base sequence of the first primer (Figure 1, top section, one strand (first strand) of double-stranded adapters) and a second end complementary to a base sequence on a first end of a bridge nucleic acid (Figure 1, first strand is also complementary to bridge sequence, the opposite strand of adapter used in blunt end ligation which increases the efficiency of ligation, column 8, lines 22-24); synthesizing a second nucleic acid that includes a first end comprising a base sequence that matches the base sequence of the second primer (Figure 1, top section, opposite strand (second strand) of double-stranded adapters) and second end complementary to a second end of the bridge nucleic acid (Figure 1, second strand is also complementary to bridge sequence, the opposite, or first strand of adapter used in blunt end ligation which increases the efficiency of ligation, column 8, lines 22-24); and making the reference nucleic acid by joining multiple nucleic acid segments in the ligation extension, including joining the first nucleic acid on one end of the joined segments using the bridge nucleic acid and joining the second nucleic acid on the opposite end of the joined segments using the bridge nucleic acid (blunt end ligation of double-stranded adapters to either end of DNA fragment, Figure 1, column 8, lines 13-32).

With regard to claim 23, Chenchik teaches a method, further comprising joining multiple nucleic acids using an overlap extension to perform the synthesizing of one or more reference nucleic acid sequences (using adapters of unequal length which can be

extended to fill in ends after annealing of strands using a DNA polymerase, Figure 2, middle section, column 8, lines 3-12).

With regard to claim 28, Chenchik teaches a method, wherein the synthesizing and the tagging include a ligation extension of two or more nucleic acids (double-stranded adapters, ligated to each end, Figure 1, top section and column 7, line 66 to column 8, line 12).

With regard to claim 71, Chenchik teaches a method, comprising: synthesizing a first mixture of various reference nucleic acids, wherein each of the various reference nucleic acids in the first mixture includes one or more tags allowing PCR amplification of the first mixture via a primer set specific to the tags of the first mixture (Figure 3, top and bottom); and synthesizing a second mixture of various reference nucleic acids, wherein each of the various reference nucleic acids in the second mixture includes one or more tags allowing PCR amplification of the second mixture via a second primer set specific to the tags of the second mixture (Figure 3, top, two mixtures using same primer sets and adapters, resulting in two populations of amplified products, bottom).

With regard to claim 72, Chenchik teaches a method, further comprising combining the first and second mixtures to make a single mixture and differentially amplifying the first mixture and the second mixture in a PCR reaction by controlling amounts of the first primer set and second primer set in the single mixture (amounts of primers are kept at equal levels, but prevented from binding to pan structures, thus leading to differential amplification of the mixtures, Figure 3 and column 14, lines 5-20).

With regard to claim 73, Chenchik teaches a method, wherein at least some of the reference nucleic acids include mutations of a normal human nucleic acid (partially homologous sequences, column 12, lines 28-30 or those with mutations, column 12, line 66 to column 13, line 8; see Example 4 for example of human nucleic acid, skeletal muscle, column 24, lines 8-25).

With regard to claim 74, Chenchik teaches a method, further comprising adding normal human nucleic acid to the single mixture to obtain heterozygous pairs, wherein each heterozygous pair includes a normal segment of human nucleic acid and a mutated copy of the normal segment of human nucleic acid (normal genomic sequences analyzed along with mutant sequences for chromosome mapping, column 12, line 66 to column 13, line 8 and Example 4 for example of human nucleic acid, skeletal muscle, column 24, lines 8-25).

4. Claims 1, 2, 4, 5, 8, 23, 71, and 72 are rejected under 35 U.S.C. 102(b) as being anticipated by Legay et al., (Vet. Res. (2000) 31: 565-572).

Legay teaches a method, comprising: synthesizing one or more nucleic acid sequences (by amplification of African Horse Sickness Virus, AHSV, by PCR, p. 567, column 1, lines 18-19), each relevant for use as a clinical reference (to be used as internal standard in biological testing for Borna Disease Virus (BDV), p. 566, column 2, line 18 to p. 567, line 6); tagging at least one end of each sequence for amplification by a primer (Figure 1, top and p. 567, column 1, line 20 to column 2, line 15); and amplifying the one or more nucleic acid sequences using the primer (column 2, line 15 to p. 568, column 1, line 20).

With regard to claim 2, Legay teaches a method, wherein the tagging includes attaching an additional sequence of nucleotides, wherein the additional sequence is complementary or identical to a nucleotide sequence of the primer (contains external and internal BDV primer sites, Figure 1, top and p. 567, column 1, line 20 to column 2, line 15).

With regard to claim 4, Legay teaches a method, wherein the tagging includes attaching a first sequence of nucleotides to a first end of each of the one or more synthesized nucleic acid sequences (Figure 1, top left side), wherein the first sequence is complementary to a nucleotide sequence of a first primer set (Table I, BDV forward primers), and the tagging includes attaching a second sequence of nucleotides to a second end of each of the one or more synthesized nucleic acid sequences (Figure 1, top right side), wherein the second sequence is identical to a nucleotide sequence of a second primer of a primer set (Table I, BDV reverse primers).

With regard to claim 5, Legay teaches a method, wherein the synthesizing comprises synthesizing two complementary nucleic acid strands (by PCR amplification of African Horse Sickness Virus using AHSV primers, p. 567, column 1, lines 18-19 and Table I), wherein: a first strand includes a first nucleic acid sequence relevant for clinical reference and a nucleic acid tag complementary to a first primer of a primer set (added by second PCR reaction, Figure 1, top left and Table I, BDV forward primers) and a second strand includes a nucleic acid sequence complementary to the first strand and a nucleic acid tag complementary to a second primer of a primer set (added by second PCR reaction, Figure 1, top right and Table I, BDV reverse primers).

With regard to claim 8, Legay teaches a method, further comprising synthesizing multiple mixtures of at least one reference nucleic acid apiece (two reference nucleic acids produced, each with different target sites within BDV; p. 566, column 2, line 32 to p. 567, column 1, line 6), wherein: each of the multiple mixtures has an associated primer set (Figure 1, top and Table 1, p40 and p24 primers), and wherein: each member of one of the multiple mixtures includes a first tag attached to a first end of the member, wherein: the first tag comprises a sequence of nucleotides complementary to a nucleotide sequence of a first primer of the associated primer set (added by second PCR reaction, Figure 1, top left and Table I, BDV forward primers), and each member includes a second tag attached to a second end of the member, wherein: the second tag comprises a sequence of nucleotides identical to a nucleotide sequence of a second primer of the associated primer set (added by second PCR reaction, Figure 1, top right and Table I, BDV reverse primers).

With regard to claim 23, Legay teaches a method, further comprising joining multiple nucleic acids using an overlap extension to perform the synthesizing of one or more reference nucleic acid sequences (using overhanging adapters which are extended during PCR to fill in ends to make fully duplex reference nucleic acid, Figure 1, middle section, p. 567, column 1, line 16 to column 2, line 15 and p. 569, column 1, lines 33-38).

With regard to claim 71, Legay teaches a method, comprising: synthesizing a first mixture of various reference nucleic acids, wherein each of the various reference nucleic acids in the first mixture includes one or more tags allowing PCR amplification of

the first mixture via a primer set specific to the tags of the first mixture (PCR amplification of AHSV sequence using primers and primer tag sites on ends of AHSV cDNA fragment, Figure 1, top and p. 567, column 1, lines 18-19) and synthesizing a second mixture of various reference nucleic acids, wherein each of the various reference nucleic acids in the second mixture includes one or more tags allowing PCR amplification of the second mixture via a second primer set specific to the tags of the second mixture (PCR amplification of AHSV fragment using mimic primers to add tags to reference nucleic acid, Figure 1, middle, and p. 567, column 1, line 20 to column 2, line 15).

With regard to claim 72, Legay teaches a method, further comprising combining the first and second mixtures to make a single mixture and differentially amplifying the first mixture and the second mixture in a PCR reaction by controlling amounts of the first primer set and second primer set in the single mixture (primers are diluted out from first PCR when added to mixture for second PCR containing full levels of primers, thus leading to differential amplification of the mixtures, Figure 1 and p. 567, column 1, line 16 to p. 568, column 1, line 10).

Conclusion

5. Claims 1, 2, 4, 5, 7-9, 11, 16, 21-23, 28, and 71-74 are rejected. No claims are allowable.

Correspondence

6. Any inquiry concerning this communication or earlier communications from the examiner should be directed to David C. Thomas whose telephone number is 571-272-3320. The examiner can normally be reached on 5 days, 9-5:30.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary Benzion can be reached on 571-272-0782. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

David C. Thomas 3/17/06
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